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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,175	09/23/2003	Nicole Zitzmann	080618-0304	1693

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FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
BROWN, TIMOTHY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/669,175	ZITZMANN ET AL.	
	Examiner	Art Unit	
	Timothy M. Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *1-41,56 and 57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/30/04; 10/13/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is responsive to the communication received July 27, 2005. Applicants' election of Group III without traverse is acknowledged. Accordingly, the status of the claims is as follows:

Claims 1-57 are pending.

Claims 42-55 are under examination.

Claims 1-41, 55 and 56 are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 42 is drawn to a method for screening for potential HCV inhibitors wherein the effect of a candidate inhibitor on the permeability of a p-7 containing membrane is compared to the permeability of p-7 containing membrane without the application of the candidate inhibitor. However, the claim lacks a resolution step wherein the increased or decreased permeability induced by the candidate inhibitor is correlated with antiviral activity. The scope of the claims is therefore indefinite.

Claim 42 is indefinite in the recitation of "a variant" in line 3. This language is indefinite in that it does not indicate whether "a variant" refers to a species of the p-7 protein, or some

other protein. Appropriate correction is required. For examination purposes, "a variant" has been interpreted to refer to a variant of the p-7 protein.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation.

Courts define undue experimentation by the following factors: the breadth of the claims; the nature of the invention; the state of the prior art; the level of one of ordinary skill; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

The breadth of Applicants' claims provide for a method of identifying antiviral agents that have potential for treating HCV infection, wherein a candidate agent's antiviral activity is confirmed by the agent's ability to decrease the permeability of a p-7 containing membrane. The specification however fails to enable such a method. This results because Applicants have not shown that p-7 controls HCV infection by modulating membrane permeability.

The state of the art at the time this application was filed showed that the role of p-7 in supporting HCV infection was unclear. In fact, even recent research has failed to identify the

function of the p-7 protein. Recent research shows that HCV p-7 mutants have decreased ability to cause infection *in vivo* (Sakai et al. PNAS (2003) 100, 20, 11646-11651). However, it is unclear whether the loss of infectivity is due to the decreased ability of the mutant p-7 protein to decrease membrane permeability. It has been suggested that the decreased infectivity of HCV p-7 mutants may be due to the interaction of the p-7 coding regions with other portions of the HCV genome (Id. at 11649, first complete paragraph). Whether membrane permeability determines HCV infectivity is also complicated by research into other viroporin proteins. This follows from experimentation that shows the ion channel protein NB from influenza B has no impact on virus propagation (Id. at 11646). Thus, the state of the art at the time the application was filed shows that there was little information available on the mechanism of p-7 in supporting HCV infection. Based on this unpredictability, one skilled in the art would have to rely heavily on the specification in reducing the claimed method to practice. The content of the specification however fails to provide any evidence that p-7 controls HCV infectivity by modulating membrane permeability. Rather, the specification simply details the synthesis and routes of administration of a variety of proposed antiviral compounds. Applicants' working examples also fail to show a correlation between a compound impact on p-7 permeability and HCV infectivity. Although Example 2.2 shows that a number of compounds have the ability to effect p-7 permeability in vitro, it fails to show that this permeability controls HCV infection.

Without the benefit of teachings in the art, or some direction in the specification, one skilled in the art would have to invest significant of experimentation in order to make and use the invention. Not only would the skilled artisan have to discover the role of membrane permeability in HCV infection, but he would also have to do so without an effective *in vitro*

model for studying HCV infection. Clearly this would go beyond routine experimentation. Therefore, one skilled in the art would have to invest undue experimentation in order to make and use the claimed invention.

Claims 42-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Here, Applicants' specification fails to provide adequate written support for a "p7 protein . . . variant." However, the specification fails to detail any variations of the p7 protein that modulate membrane permeability. Applicants have not disclosed the specific sequences, motifs or regions of the p-7 peptide that give the peptide its porin activity. Rather, the specification only details the permeability of the entire p-7 protein. The state of the art at the time this application was filed also fails to suggest that the inventors were in possession of the range of p-7 peptides claimed; the art did not teach those regions of the p-7 protein that control membrane permeability. Accordingly, one skilled in the art could not reasonably conclude that the inventors were in possession of the claimed invention at the time this application was filed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy M. Brown whose telephone number is (571) 272-0773. The examiner can normally be reached on Monday - Friday, 8am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Timothy M. Brown
Examiner
Art Unit 1648

tmb

JAMES HOUSEL 10/31/05
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

TMB 10/31/05